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**Engineered stem cell mimics to enhance stroke recovery.**

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**Public Summary:**

Currently, no medical therapies exist to augment stroke recovery. Stem cells are an intriguing treatment option being evaluated, but cell-based therapies have several challenges including developing a stable cell product with long term reproducibility. Since much of the improvement observed from cellular therapeutics is believed to result from trophic factors the stem cells release over time, biomaterials are well-positioned to deliver these important molecules in a similar fashion. Here we show that essential trophic factors secreted from stem cells can be effectively released from a multi-component hydrogel system into the post-stroke environment. Using our polymeric system to deliver VEGF-A and MMP-9, we improved recovery after stroke to an equivalent degree as observed with traditional stem cell treatment in a rodent model. While VEGF-A and MMP-9 have many unique mechanisms of action, connective tissue growth factor (CTGF) interacts with both VEGF-A and MMP-9. With our hydrogel system as well as with stem cell delivery, the CTGF pathway is shown to be downregulated with improved stroke recovery.

**Scientific Abstract:**

Currently, no medical therapies exist to augment stroke recovery. Stem cells are an intriguing treatment option being evaluated, but cell-based therapies have several challenges including developing a stable cell product with long term reproducibility. Since much of the improvement observed from cellular therapeutics is believed to result from trophic factors the stem cells release over time, biomaterials are well-positioned to deliver these important molecules in a similar fashion. Here we show that essential trophic factors secreted from stem cells can be effectively released from a multi-component hydrogel system into the post-stroke environment. Using our polymeric system to deliver VEGF-A and MMP-9, we improved recovery after stroke to an equivalent degree as observed with traditional stem cell treatment in a rodent model. While VEGF-A and MMP-9 have many unique mechanisms of action, connective tissue growth factor (CTGF) interacts with both VEGF-A and MMP-9. With our hydrogel system as well as with stem cell delivery, the CTGF pathway is shown to be downregulated with improved stroke recovery.

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